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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/784,452	02/23/2004	Jeffrey J. Cernohous	55970US008	9990

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EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	

NOTIFICATION DATE	DELIVERY MODE
12/02/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/784,452	CERNOHOUS ET AL.	
	Examiner	Art Unit	
	TERESA WESSENDORF	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/5/08 has been entered.

Status of the Claims

Claims 1-22 were pending.

Claims 21 is drawn to non-elected species and/or inventions and thus this claim remains withdrawn from further consideration by the examiner, 37 CFR 1.142(b), there being no allowable generic claim.

Claims 1-20 and 22 are examined in this action.

Specification

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: the sequential steps of claims 1, 10, 20 and 22.

Withdrawn Rejections

In view of applicants' arguments the 35 USC 102 rejection is withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-20 and 22, as amended, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. In claims 1, 10, 20 and 22 the recitation of a "sealed flexible polymer pouches" is incontinent with the specification (e.g., page 3) which recites a **fluid impervious**, sealed flexible polymer pouches. It would appear that the fluid impervious feature is essential to the claimed pouch especially if the reaction zone, as disclosed in the specification is a water bath.

2. There is a lack of correspondence between the preamble in claim 1, for example, and the body of the claim. The preamble recites for the synthesis of an array of **polymer**. The body of the claim recites **first and second reactants**. If these are the

same thing, then the used of different terminologies provide for confusion and ambiguity. While applicants are permitted to be his own lexicographer however, it carries with it the connotation that he will use terms consistently throughout his patent. Porter v. Farmers Supply Services Inc., 228 USPQ 4.

This rejection has the same import to claims 10, 20 and 22.

3. Claim 1 is unclear as to the recitation of a "same" first reactant and a "same" second reactant especially in the absence of positive support in the specification. If the reactants are the same, is the polymer a single chain of monomers, for example, the amino acid alanine (ala) linked together to form an (ala)n polymer?

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 103

Claims 1-20 and 22, as amended, are rejected under 35 U.S.C. 103(a) as being unpatentable over Neukermans (WO 97/22825) (Date of Patent is June 26, I997) in view of McPherson et al. (PCR. M. J. McPherson and S. G. Moller. BIOS Scientific Publishers, Oxford. 2000, pages 9-21 and 67-87) for reasons of record as reiterated below.

For claim 1, Neukermans discloses a method for the synthesis of an array of polymers (e.g., see abstract; see also

pages 20 and 21 which results in the synthesis of an array of DNA via PCR). Neukermans et al. further disclose (a) providing an array of sealed flexible polymeric pouches (e.g., see figures 3 and 4 wherein the pouches are elements 124a, 124b, and 124c and/or 122; see also figure 11 wherein the pouches are elements 128 connected in series; see also page 21, first full paragraph; see also page 11, last paragraph wherein polyethylene/polyimide is disclosed as the material for making the pouch; see also page 14, last paragraph, pouch 108 is preferably made from ... flexible ... polymeric sheets; see also page 22, last paragraph disclosing thickness in the range of 0.001 inch; see also page 13, last paragraph; see also page 26, paragraph wherein a single sheet is used). Furthermore, Neukermans et al. disclose that each pouch attached to a conveyance apparatus (e.g., see figure 3 elements 158a, 158b, 158c or, alternatively, elements 128a, 128b, and 128c; elements 146 used in conjunction with elements 124a, 124b, and 124c may also be considered separately or together as part of the conveyance apparatus; see also figures 1 and 2 wherein element 24 may be considered part of the conveyance apparatus; see also page 16, paragraphs 1 and 2 wherein the peristaltic pump/syringe may be considered part of the conveyance apparatus). Neukermans also discloses that each pouch contains a first reactant and a same second reactant

(e.g., see figure 11; see also pages 21 and 22 wherein reagents for PCR are set forth for the two reaction chambers shown in figure 11, which would include the DNA, heat stable polymerase, primers, etc. any of which would qualify as first/second reagents). Neukermans also discloses (b) conveying the array of sealed flexible polymeric pouches through a reaction zone to cause the first reactant in each pouch to react with the second reactant in each pouch to produce an array of polymers (e.g., see figure 11; processing chambers 198; see also page 21, last paragraph, especially lines 26-27, "Temperature cycling can be accomplished by heating or cooling the processing chambers 198 [i.e., reaction zones], or, preferably, by periodically shuttling the liquid back and forth between the processing chambers 198 while maintaining the processing chambers 198 respectively at the two PCR temperatures"). More specifically, as shown in figure 11, the pouches are "conveyed" from one location to another by the "compression" of the peristaltic pumps (shown as elements 202 in figure 11 a) relative to the reaction chambers 196 (see also paragraph bridging pages 21 and 22, "the piezoelectric transducers alternatively press the pistons 202 down first onto one of the processing chambers 198 and then onto the other processing chamber 198 [i.e., processing chambers 198 are "conveyed" from one place to another] ... To

enhance temperature uniformity while performing PCR, the pistons 202 may also be maintained at the temperatures T 1 and T2 required for PCR"). Alternatively, page 19, first full paragraph discloses the "conveyance" of portable microfluidic systems into the appropriate reaction zones and their subsequent alignment via registration pins 106 (see also page 26). Finally, the method disclosed by Neukermans could be viewed as a "continuous" because the PCR reaction is "continually" performed via the requisite number of cycles to make the final product (e.g., see page 22, lines 8-9, "After performing the requisite number of cycles to complete PCR, the product thus obtained may be transferred through the capillary 126 to its ultimate destination"). For claim 2, Neukermans discloses the method according to claim 1 wherein the providing step further comprises providing an array of pouches that are linearly joined (e.g., see figure 11; elements 196/198 are linearly joined; see also figure 5 and discussion related thereto). For claim 3, Neukermans discloses the method according to claim 1 wherein the providing step further comprises providing an array of pouches that are linearly and horizontally joined (e.g., see figure 3-5 and 11 showing both linear and horizontal arrangements). For claim 4-6, Neukermans discloses the method according to claim 1 conveying the array of sealed flexible polymeric pouches through

a reaction zone to cause the first reactant in each pouch to react with the second reactant in each pouch to produce an array of 90 different polymers (e.g., see page 19, first full paragraph disclosing the conveyance of portable microfluidic systems that are subsequently aligned via the registration pins 106 to insure that the pouches pass into the appropriate reaction zones; see also page 26). Neukermans do not state that 90 different polymers are produced but the Examiner contends that this would be an inherent feature of the PCR process as an enormous number of copies of the DNA are produced during the course of the synthesis including from 1 to 1,048,576 copies by the 20th cycle (e.g., see McPherson et al., page 12, Table 2.1), which would include 10, 30 and 90 along the way. For claim 7, Neukermans discloses the method according to claim 1 further comprising the step of labeling each pouch (e.g., see figures 3-5 wherein the pouches are labeled with element numbers). For claim 9, Neukermans discloses the method according to claim 1 further comprising the step of analyzing the polymer in each sealed flexible polymeric pouch by a non-destructive technique (e.g., see figure 12; see also page 23, paragraph 1 wherein non-destructive fluorescence analysis is disclosed; see also page 23, paragraph 2 wherein TIR is disclosed; see also figure 15 wherein CE is disclosed). For claim 10, Neukermans further

discloses, in addition to the limitations set forth above for claim 1, the use of a captive pouch. For instance, element 108 may be viewed as "large" pouch in figure while elements 124a, 124b, 124c, 122, etc may be viewed as the "captive" pouches. Furthermore, the duplication of the large pouches to process multiple samples in parallel would be immediately envisioned. See, for example, In re Harza, (274 F.2d 669, 124 USPQ 378 (CCPA 1960)) where the court held that mere duplication of parts has no patentable significance unless a new and unexpected result is produced. For claim 11, Neukermans discloses the method according to claim 10 wherein the step of providing comprises providing a captive pouch containing a portion of the same first reactant or a portion of the same second reactant (e.g., see figure 11 wherein from 1 to 1,048,576 copies by the 20th cycle (e.g., see McPherson et al., page 12, Table 2.1), which would include 10, 30 and 90 along the way. For claim 7, Neukermans discloses the method according to claim 1 further comprising the step of labeling each pouch (e.g., see figures 3-5 wherein the pouches are labeled with element numbers). For claim 9, Neukermans discloses the method according to claim 1 further comprising the step of analyzing the polymer in each sealed flexible polymeric pouch by a non-destructive technique (e.g., see figure 12; see also page 23, paragraph 1 wherein non-

destructive fluorescence analysis is disclosed; see also page 23, paragraph 2 wherein TIR is disclosed; see also figure 15 wherein CE is disclosed). For claim 10, Neukermans further discloses, in addition to the limitations set forth above for claim 1, the use of a captive pouch. For instance, element 108 may be viewed as "large" pouch in figure while elements 124a, 124b, 124c, 122, etc may be viewed as the "captive" pouches. Furthermore, the duplication of the large pouches to process multiple samples in parallel would be immediately envisioned. See, for example, In re Harza, (274 F.2d 669, 124 USPQ 378 (CCPA 1960)) where the court held that mere duplication of parts has no patentable significance unless a new and unexpected result is produced. For claim 11, Neukermans discloses the method according to claim 10 wherein the step of providing comprises providing a captive pouch containing a portion of the same first reactant or a portion of the same second reactant (e.g., see figure 11 wherein the liquid is shuttled back and forth and, as a result, each pouch contains a "portion" of the reagents at any one given time; see also page 21, last paragraph). For claim 12, Neukermans discloses the method according to claim 10 wherein the step of providing comprises providing a captive pouch containing a third reactant that is different than the first or second reactant (e.g., see figure 3 showing pouches for three

different reactants; see also figure 5 showing pouches for 4 different reactants corresponding to elements 124a-d). For claim I3, Neukermans discloses the method according to claim 10 further comprising the step of rupturing the captive pouch and releasing material within the captive pouch into the each sealed flexible polymeric pouch (e.g., see figure 7 wherien the rupturing occurs by applying an electric voltage to the piezoelectric element thereby rupturing the seal between elements 114 and 116). For claim I4, Neukermans discloses the method according to claim 13 wherein the rupturing step precedes the exposing step (e.g., see figure 3 wherein the rupturing that occurs during the piezoelectric valve switch precedes a heat exposure to element 122 via element 152). For claim I5, Neukermans discloses the method according to claim 13 wherein the rupturing step follows the exposing step (e.g., see figure 11 wherein the processing chambers are exposed to heat, etc. and then ruptured via another piezoelectric valve; see also figure 10 and corresponding text wherein many different configurations are disclosed). For claim I6, Neukermans discloses the method according to claim 15 further comprising the step of exposing the ruptured pouches to a controlled environment to cause the material within the captive pouch to react with the polymer in each sealed polymeric pouch (e.g., see figure 11 wherein the

pouches are exposed to a controlled environment such as conditions amenable to PCR; see also page 21, last two paragraphs). For claim 17, Neukermans discloses the method according to claim 10 wherein the step of providing comprises providing a captive pouch attached to each sealed flexible polymeric pouch (e.g., see figure 3 wherein the pouch 108 contains a captive pouch such as 124, 128 or 122; see also figure 5 showing captive pouches 124a-d). Please note that merely "duplicating" the number of pouches (i.e., element 108), which contain various captive pouches; to process more than one sample in parallel is not inventive. See, for example, In re Harza, (274 F.2d 669, 124 USPQ 378 (CCPA 1960)) where the court held that mere duplication of parts has no patentable significance unless a new and unexpected result is produced. For claim 18, Neukermans discloses the method according to claim 10 wherein the step of providing comprises providing a captive pouch free floating within each sealed flexible polymeric pouch (e.g., see page 15, first full paragraph, especially lines 15-16, "Entire areas of the sheets 114 and 116 may be laminated, or laminations may be formed only partially to outline the patterns [i.e., freely floating with respect to the parts that are not laminated]"; see also page 17, last paragraph, "It is not necessary to laminate together the entire areas outside of the

reservoirs ... Laminating the peripheries of these areas is sufficient"). For claim 19, Neukermans discloses the method according to claim 10 wherein the step of providing comprises providing more than one captive pouch within each sealed flexible polymeric pouch (e.g., see figures 3 and 5 disclosing more than one captive pouch).

For claim 20, Neukermans (see entire document) discloses a method for the synthesis of an array of polymers (e.g., see abstract; see also pages 20 and 21 which results in the synthesis of an array of DNA via PCR). Neukermans further discloses (a) providing an array of sealed flexible polymeric pouches (e.g., see figures 3 and 4 wherein the pouches are elements 124a, 124b, and 124c and/or 122; see also figure 11 wherein the pouches are elements 128 connected in series; see also page 21, first full paragraph; see also page 11, last paragraph wherein polyethylene/polyimide is disclosed as the material for making the pouch; see also page 14, last paragraph, pouch 108 is preferably made from ... flexible ... polymeric sheets; see also page 22, last paragraph disclosing thickness in the range of 0.001 inch; see also page 13, last paragraph; see also page 26, paragraph wherein a single sheet is used). Neukermans further discloses that each pouch attached to a conveyance apparatus (e.g., see figure 3 elements 158a, 158b,

158c or, alternatively, elements 128a, 128b, and 128c; elements 146 used in conjunction with elements 124a, 124b, and 124c may also be considered separately or together as part of the conveyance apparatus; see also page 16, paragraphs 1 and 2 wherein the peristaltic pump/syringe may be considered part of the conveyance apparatus). Neukermans also discloses that each pouch containing a same first reactant and a same second reactant (e.g., see figure 11; see also pages 21 and 22 wherein reagents for PCR are set forth for the two reaction chambers [i.e., pouches] shown in figure 11 corresponding to elements 198, which would include the DNA, heat stable polymerase, primers, etc. any of which would qualify as first/second reagents). Neukermans also discloses that at least a first pouch and a second pouch contains a similar volume ratio of first reactant to second reactant (e.g., see figure 11 wherein the contents of one chamber is shuttled back and forth to another second reaction chamber which would contain the same volume ratio of first reactant to second reactant before during and after the transport; see also page 21, last paragraph, especially, lines 26-30). Neukermans also discloses (b) conveying the array of sealed flexible polymeric pouches through a reaction zone exposing the first pouch to a first set of reaction conditions and exposing the second pouch to a second

set of reaction conditions where the first set of reaction conditions are different than the second set of reaction conditions and cause the first reactant in each pouch to react with the second reactant in each pouch to produce an array of polymers (e.g., see figure 11; processing chambers 198; see also page 21, last paragraph, especially lines 26-27, "Temperature cycling can be accomplished by heating or cooling the processing chambers 198 [i.e., reaction zones], or, preferably, by periodically shuttling the liquid back and forth between the processing chambers 198 while maintaining the processing chambers 198 respectively at the two PCR temperatures [i.e., the chambers are kept at two different temperatures, or reaction conditions, and the liquid is cycled back and forth between the two]"). More specifically, as shown in figure 11, the pouches are "conveyed" from one location to another by the "compression" of the peristaltic pumps (shown as elements 202 in figure 11 a) relative to the reaction chambers 196 (see also paragraph bridging pages 21 and 22, "the piezoelectric transducers alternatively press the pistons 202 down first onto one of the processing chambers 198 and then onto the other processing chamber 198 [i.e., processing chambers 198 are "conveyed" from one place to another] ... To enhance temperature uniformity while performing PCR, the pistons 202 may also be maintained at

the temperatures T 1 and T2 required for PCR"). Alternatively, page 19, first full paragraph discloses the "conveyance" of portable microfluidic systems into the appropriate reaction zones and their subsequent alignment via registration pins 106 (see also page 26). Finally, the method disclosed by Neukermans could be viewed as a "continuous" because the PCR reaction is "continually" performed via the requisite number of cycles to make the final product (e.g., see page 22, lines 8-9, "After performing the requisite number of cycles to complete PCR, the product thus obtained may be transferred through the capillary 126 to its ultimate destination").

For claim 22, Neukermans discloses in addition to the limitations set forth in claim 1, the use of a first and second reactant polymer (e.g., the primers or the template DNA strand) and also the use of a mixing chamber (e.g., see figure 11 wherein the liquid is shuttled back and forth or "tapped" periodically with a piston (e.g., see figure 11; see also page 22, paragraphs 1 and 2). The prior art teachings of Neukermans differ from the claimed invention as follows: For claims 1 and 8, Neukermans fails to teach different volume ratio of first/ second reactants. Neukermans is silent on this point only mentioning that PCR is performed via thermocycling in the array of pouches disclosed therein. However, McPherson et al. teach

the following limitations that are deficient in Neukermans: For claims 1 and 8, McPherson et al. (see chapters 2 and 4) teach the use of PCR and optimization protocols related thereto. Specifically, McPherson et al. teach the use of adding different amounts/volumes of template, primer, reaction additives and enzyme to optimize PCR reactions that don't produce any product or, alternatively, produce too many products indiscriminately (e.g., see chapter 2 for general PCR setup and background; see chapter 4 for optimization, especially section 2.3, 2.10, 3 and table 4.1 disclosing various optimization protocols wherein the amount of one or more reagent is varied; see also section 2.3 with regard to setting up multiple samples (i.e., a titration) in parallel to test various amounts of a reagent). It would have been prima-facie obvious to one of ordinary skill in the art at the time the invention was made to use different volumes/amounts of PCR reagents as taught by McPherson et al. in the PCR method/apparatus as taught by Neukermans because McPherson et al. explicitly states that PCR methods often require optimization. Furthermore, a person of ordinary skill in the art would have been motivated to use the optimization conditions set forth in McPherson et al. to obtain the desired quantity of DNA product in cases where the "standard" conditions were not sufficient. In addition, a person of skill in the art would have

been motivated to test more than one sample in parallel to increase the speed by which a large number of optimization conditions could be tested in a given period of time. A person of skill in the art would reasonably have expected to be successful because PCR is a widely used, routine technique employing "text book" optimization protocols (e.g., see McPherson et al., Table 4.1).

Response to Arguments

Applicants state that reaction chambers 198 of Neukermans are not conveyed, but rather attached to a support. It is further argue that the individual flexible pouches of the present application are reaction vessels (page 6, lines 13-14) conveyed through a reaction zone. Neukermans discloses conveying materials of reaction chambers 198 between reaction zones T1 and T2 with applied pressure from pistons 202. Neukermans does not convey sealed flexible polymeric pouches with a conveyance apparatus of the present application. Neukermans fails to disclose a conveyance apparatus that conveys the array of sealed flexible polymeric pouches through a reaction zone exposing the first pouch to a first set of reaction conditions and exposing the second pouch to a second set of reaction conditions.

In response, the claims do not preclude the argued support. In using the word "comprising" the claimed does not preclude the

presence of other components present in the prior art formulation. It has been long held that the use of the term "comprising' leaves a claim open for inclusion of materials or steps other than those recited in the claims". Ex parte Davis, 80 USPQ 448. Nonetheless, attention is drawn for example to Figs. 2 and 4, which discloses a free standing array of pouches.

In addition, elements 124/122 permit the use of PCR reactions to take place and thus are made of materials that are impervious to fluids in the surrounding environment and inert to materials within it (e.g., see paragraph bridging pages 11 and 12. Clearly, a peristaltic pump or the valve assemblies shown in the figures "convey" these types of materials from one place to another and Applicants admit as much when they state on the top of page 10 of the 3/5/08 response, "Neukermans describes liquids which are conveyed from more than one reservoir using external microfluidic valve(s) to control the flow of the liquids into the capillaries flowing into a reaction chamber." Claims are to be given their broadest reasonable interpretation consistent with Applicants' specification (e.g., see In re Zletz, 13 USPQ2d 1320, 1322 (Fed Cir. 1989) (holding that claims must be interpreted as broadly as their terms reasonably allow); MPEP § 2111. Given this standard, the word "convey" is held here to mean simply moving something from one location to another. In

the context of the claims, that would mean a physical movement of the pouches from one location to another with the caveat that the pouches move through a reaction zone. Here, figure 11 a clearly depicts movement of the pouches (via elements 202) through reaction zones T1 and T2. This is further supported by the accompanying text which reads in pertinent part, "the piezoelectric transducers alternatively press the pistons 202 down first onto one of the processing chambers 198 and then onto the other processing chamber 198 ... To enhance temperature uniformity while performing PCR, the pistons 202 may also be maintained at the temperatures T1 and T2 required for PCR" (e.g., see paragraph bridging pages 21 and 22). Thus, reaction chambers 198 are conveyed (i.e., moved from one place to another) through the reaction zones (i.e., reaction zones T1 and T2 formed from the pistons, which may be heated/cooled, and the heating/cooling elements 196). Alternatively, the pouches are also "conveyed" when they are placed into the apparatus and aligned with heating/cooling elements via the registration pins (e.g., see page 19, first full paragraph disclosing the conveyance of portable microfluidic systems that re subsequently aligned via the registration pins 106 to insure that the pouches pass into the appropriate reaction zones; see also page 26.

Accordingly, pouches are used in the art to synthesize library of monomers. Whether the pouches are attached to a conveyor (i.e., automatic) or not e.g., manually operated would produce the same, if not similar result of synthesis of the polymers. Please note however, that Nuckermans teaches also the same, if note similar, automation process using pouch for combinatorial synthesis of monomers.

Applicants recognize that McPherson describes a polymerase chain reaction (PCR) as a technique for in vitro amplification of specific DNA sequences by the simultaneous primer extension of complimentary strands of DNA to produce numerous copies of DNA (page 1 of McPherson). But argue that McPherson fails to disclose continuous methods for synthesizing an array of polymers (claims 1, 10, and 20) or polymer mixtures (claim 22) by the methods described in claims 1, 10, 20, and 22 of the present application. In the above referenced claims, McPherson does not teach or suggest providing an array of sealed flexible polymeric pouches where each pouch is attached to a conveyance apparatus that conveys the array of sealed flexible polymeric pouches. Further, McPherson does not describe conveying the array of sealed flexible polymeric pouches through a reaction zone.

In reply, McPherson is employed not for the purpose as argued. Rather for its teachings of the use of adding different amounts/volumes of template, primer, reaction additives and enzyme to optimize PCR reactions that don't produce any product or, alternatively, produce too many products indiscriminately (e.g., see chapter 2 for general PCR setup and background; see chapter 4 for optimization, especially section 2.3, 2.10, 3 and table 4.1 disclosing various optimization protocols wherein the amount of one or more reagent is varied; see also section 2.3 with regard to setting up multiple samples (i.e., a titration) in parallel to test various amounts of a reagent). Nuckermans teaches the continuous methods for synthesis of an array of polymers. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See In re Keller, 642 F.2d 413,208 USPQ 871 (CCPA 1981); In re Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Here, the combined references of Neukermans and McPherson et al. teach all of the claimed limitations as set forth in the rejection above.

> When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability. For the same reason, if a technique has been used to improve one device, and a person of ordinary skill in the art would

recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill. When considering obviousness of a combination of known elements, the operative question is thus "whether the improvement is more than the predictable use of prior art elements according to their established functions." KSR International Co. v. Teleflex Inc., 550 USPQ2d 1385 (2007).

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

1. Nova et al (USP 6284459) discloses methods in which matrices that are in the form of containers are typically used for solid phase syntheses of combinatorial libraries or as pouches.

2. Cargill et al (5770455) discloses methods and apparatus for synthesizing labeled combinatorial chemistry libraries.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TERESA WESSENDORF whose telephone number is (571)272-0812. The examiner can normally be reached on flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/TERESA WESSENDORF/
Primary Examiner, Art Unit 1639